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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,245	12/07/2001	Paul J. Carter	P0927C2	8478

9157 7590 10/19/2004

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EXAMINER	
GUCKER, STEPHEN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/010,245	CARTER ET AL.	
	Examiner	Art Unit	
	Stephen Gucker	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *1-23 and 29-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/7/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-23 and 29-38, drawn to a method of preparing a heteromultimer comprising a first polypeptide and a second polypeptide which meet at an interface, and host cells, classified in class 435, subclass 69.1+ for example.

II. Claims 24-28, drawn to a heteromultimer comprising a first polypeptide and a second polypeptide which meet at an interface, and compositions comprising such, classified in class 514/12 and 530/350+ for example.

2. Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the product of Invention II can be made by fusing two separate cells together to make a hybrid cell without resorting to the introduction into a single host cell of nucleic acid, as is the case with Invention I. Alternately, the product of Invention I can be made by using two separate host cells, introducing nucleic acids into both of them, recovering the products from both of them, and then combining the separate products under appropriate conditions to make the

final product (heteromultimer). In addition, certain small heteromultimers could be made by producing the separate peptide chains by classical peptide chemistry and then combining the separate products under appropriate conditions to make the final product (heteromultimer).

3. Because these inventions are distinct for the reasons given above, and because the search and examination of these groups are different, restriction for examination purposes as indicated is proper because the search and examination of these groups is different and would pose an undue burden to the examiner.

4. During a telephone conversation with Craig G. Svoboda on 10/6/04, a provisional election was made with traverse to prosecute the invention of Invention II, claims 24-28. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-23 and 29-38 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re

Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 24-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 5,821,333. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from

each other because the patented claims are a sub-genus of the instant generic claims, and therefore anticipate the instant generic claims.

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 24-27 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 24-27 read on antibodies, which are products of nature that occur naturally and do not show the "hand of man". The grounds of this rejection may be obviated by amending the claims to recite "an isolated heteromultimer".

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 24-28 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kostelny et al., Journal of Immunology:148, 1547-1553 (1992) (Reference 18 of PTO-1449, filed 12/7/01). Kostelny et al. teach a bispecific antibody heteromultimer comprising a first and second polypeptide which meet at an interface, wherein the interface of the first polypeptide comprises a protuberance created by a helix of a leucine zipper motif, which is positionable into a cavity created by a complementary leucine zipper helical interface of the second polypeptide. To create this set of protuberance-and-cavity-containing polypeptides, plasmid comprising native genomic

nucleic acid sequence encoding mouse IgG2a was altered via PCR to comprise the C_H1 and hinge constant domains from IgG2a fused to nucleic acid replacing C_H3 sequence and encoding the Fos or Jun leucine zipper domains. The leucine zipper sequences used by Kostelny et al. are disclosed in Landschultz et al. Science:240, 1759-1764 (1988) (Reference 19 of PTO-1449, filed 12/7/01). Arginine, an amino acid with a relatively large R group, is present on the Jun amino acid sequence, creating a protuberance. Smaller amino acid residues such as alanine, but not cysteine, are present in the fos-encoding sequence (see Fig. 2 of Landschultz et al. in particular), creating a cavity into which the arginine-containing protuberance can fit. The method includes the sequential introduction of these nucleic acid constructs (also comprising two V_H domains, see in particular Fig. 2) and L-chain plasmids to encode anti-CD3-Fos and anti-Tac-Jun to a murine myeloma cell line. Bispecific antibody secreted into the culture media was harvested and identified via anti-CD3 and anti-Tac activity.

12. The use of the trademarks such as: PRIMATIZED page 15, line 25 and page 16, line 16; INSIGHT page 38, line 2; has been noted in this application. They should be completely capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Each letter of the trademarks must be capitalized. See MPEP 608.01 (V) and Appendix I.

13. Claim 24 is objected to as being dependent upon a non-elected base claim.

14. No claim is allowed.

15. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technical Center 1600 general number which is (571) 272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (571) 272-0883. The examiner can normally be reached on Monday to Friday from 0930 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961. The fax phone number for this Group is currently (703) 872-9306.

Stephen Gucker

October 13, 2004

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600